Stromal cell-derived factor 1

The stromal cell-derived factor 1 (SDF1), also known as C-X-C motif chemokine 12 (CXCL12), is a chemokine protein that in humans is encoded by the CXCL12 gene on chromosome 10. It is ubiquitously expressed in many tissues and cell types. Stromal cell-derived factors 1-alpha and 1-beta are small cytokines that belong to the chemokine family, members of which activate leukocytes and are often induced by proinflammatory stimuli such as lipopolysaccharide, TNF, or IL-1. The chemokines are characterized by the presence of 4 conserved cysteines that form 2 disulfide bonds. They can be classified into 2 subfamilies. In the CC subfamily, the cysteine residues are adjacent to each other. In the CXC subfamily, they are separated by an intervening amino acid. The SDF1 proteins belong to the latter group. CXCL12 signaling has been observed in several cancers.

The CXCL12 gene also contains one of 27 SNPs associated with an increased risk of coronary artery disease.

Some chemokine networks, like the CXCL12/CXCR4 axis, are upregulated by tissue inflammation.

It is crucial and clinically relevant to clarify the homing efficiency and retention of stem cells in different implanting strategies of cell therapy for various injuries. However, the need for a tool for investigating the mechanisms is still unmet. Tang et al. introduced multi-modal BaGdF5:Yb, Tm nanoparticles as a nanoprobe to label adipose-derived stem cells (ADSCs) and detect the homing behavior with micro-computed tomography (micro-CT) imaging technique. The migration of cells injected locally or intravenously, with or without a chemokine, CXCL12, was compared. Higher homing efficiency of ADSCs was observed in both intravenously injected groups, in contrast to the low efficiency of cell retention in local implantation. Meanwhile, CXCL 12 promoted the homing of ADSCs, especially in the intravenous route. Nonetheless, the administration of CXCL 12 showed its therapeutic efficacy, whereas intravenous injection of ADSCs almost did not. Our work provided a tool for in vivo imaging of the behavior of implanted cells in preclinical studies of cell therapy, and more importantly, implied that the parameters for implanting stem cells in clinical operation should be carefully considered [1)].

CXCL12, a potent chemoattractant for CXCR4-expressing NSPCs, was upregulated in the ischemic lesion of N-PRβ-KO mice [2)].

The chemokine CXCL12 (also termed SDF-1, stromal cell-derived factor-1) and its receptors CXCR4 and CXCR7 are known to play a pivotal role in tumor progression including glioblastomas (Glioblastoma).

The glioma recurrence pattern is related to CXCL12 expression levels in vascular endothelial cells and CXCR4 expression levels in tumor cells; thus, implicating the CXCL12/CXCR4 signaling pathway as a potential target for glioma therapy [3)].

CXCL12 G801A polymorphism is a risk factor that increases susceptibility to gliomas in a subset of the general Han Chinese population [4)].

The CXCL12/CXCR4/PI3K/pAkt signalling pathway increased progesterone-induced endothelial progenitor cells (EPCs) viability [5].

CXCL12/CXCR4 has been demonstrated to be involved in cell proliferation, cell migration, cell invasion, angiogenesis, and radioresistance in glioblastoma (Glioblastoma). However, its role in temozolomide resistance in Glioblastoma is unknown. Wang et al. aimed to evaluate the role of CXCL12/CXCR4 in mediating the TMZ resistance to Glioblastoma cells and explore the underlying mechanisms. They found that the CXCL12/CXCR4 axis enhanced TMZ resistance in Glioblastoma cells. Further study showed that CXCL12/CXCR4 conferred TMZ resistance and promoted the migration and invasion of Glioblastoma cells by up-regulating FOXM1. This resistance was partially reversed by suppressing CXCL12/CXCR4 and FOXM1 silencing. This study revealed the vital role of CXCL12/CXCR4 in mediating the resistance of Glioblastoma cells to TMZ, and suggested that targeting CXCL12/CXCR4 axis may attenuate the resistance to TMZ in Glioblastoma [6].

1)
Tang N, Wang X, Zhu J, Sun K, Li S, Tao K. Labelling stem cells with a nanoprobe for evaluating the homing behaviour in facial nerve injury repair. Biomater Sci. 2022 Jan 6. doi: 10.1039/d1bm01823j. Epub ahead of print. PMID: 34989358.
2)
Sato H, Ishii Y, Yamamoto S, Azuma E, Takahashi Y, Hamashima T, Umezawa A, Mori H, Kuroda S, Endo S, Sasahara M. PDGFR-β Plays a Key Role in the Ectopic Migration of Neuroblasts in Cerebral Stroke. Stem Cells. 2015 Oct 4. doi: 10.1002/stem.2212. [Epub ahead of print] PubMed PMID: 26435273.
3)
Tang W, Wang X, Chen Y, Zhang J, Chen Y, Lin Z. CXCL12 and CXCR4 as predictive biomarkers of glioma recurrence pattern after total resection. Pathol Biol (Paris). 2015 Sep;63(4-5):190-8. doi: 10.1016/j.patbio.2015.07.002. Epub 2015 Aug 14. PubMed PMID: 26277915.
4)
Chang SF, Li SL, Yang B, Yao KM, Miao RH, Liang GF, Zhang KM. CXCL12 G801A polymorphism and susceptibility to glioma: a case-control study. Genet Mol Res. 2015 Dec 21;14(4):17399-405. doi: 10.4238/2015.December.21.9. PubMed PMID: 26782381.
5)
Yu P, Zhang Z, Li S, Wen X, Quan W, Tian Q, Chen J, Zhang J, Jiang R. Progesterone modulates endothelial progenitor cell (EPC) viability through the CXCL12/CXCR4/PI3K/Akt signalling pathway. Cell Prolif. 2016 Jan 27. doi: 10.1111/cpr.12231. [Epub ahead of print] PubMed PMID: 26818151.
6)
Wang S, Chen C, Li J, Xu X, Chen W, Li F. The CXCL12/CXCR4 axis confers temozolomide resistance to human glioblastoma cells via up-regulation of FOXM1. J Neurol Sci. 2020 Apr 14;414:116837. doi: 10.1016/j.jns.2020.116837. [Epub ahead of print] PubMed PMID: 32334273.